Citation:

Mennella JA, Pepino MY. Breast pumping and lactational state exert differential effects on ethanol pharmacokinetics. Alcohol. 2010; 44 (2): 141-148.

PubMed ID: 20056373

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether breast pumping worked synergistically with the physiological and metabolic changes that accompanied lactation in the metabolism of alcohol; to assess alcohol pharmacokinetics and alcohol-induced temperature changes in the same women while they were lactating and after lactation had ceased.

Inclusion Criteria:

Lactating women who were exclusively breastfeeding three- to five-month-old infants.

Exclusion Criteria:

- Smoking
- Pregnancy
- Lifetime alcohol abstinence
- Alcohol dependence
- Diabetes
- Obesity.

Description of Study Protocol:

Recruitment

12 women when they were exclusively breastfeeding three- to five-month-old infants, and then several months again after their lactation ceased.

Design

Randomized controlled trial.

Dietary Intake/Dietary Assessment Methodology:

Subjects drank 0.4g per kg dose of alcohol as well as a standard meal during one session with 530 calories.

Blinding Used

Not applicable.

Intervention

Breast pumping: One group breast pumped 0.6 hours after drinking (pumped after group, PA) and the other pumped one hour before drinking (pumped before group, PB)

Statistical Analysis

- Separate mixed analysis of variance with group (PA and PB): Conducted as the between-subjects factor and food condition (fed and fasted), reproductive stage (during lactation and after lactation), and time since alcohol consumption (when applicable) as the within-subject factors.
- If the ANOVAs revealed significant effects or interactions, post hoc Fisher least significant difference analysis were conducted.
- The critical value for significance was $P<0.05$.

Data Collection Summary:

Timing of Measurements

- Two groups of women were tested on two days separated by one week at two time periods: During and after lactation. Conditions were the same during both time periods. At time zero, women drank a 0.4g per kg body weight dose of alcohol following a 12-hour overnight fast during one test session (fasted condition) or one hour after the consumption of a standard breakfast during the other (fed condition). Group pumped before breast pumped for 16 minutes one hour before circles, while group pumped after breast pumped for 16 minutes

beginning 35 minutes (0.6 hour) after (triangles) drinking alcohol.
- BrAc measured at fixed intervals before (-90, zero minutes) and after (25, 35, 45, 55, 65, 75, 85, 95, 105, 115, 125, 135, 145, 175, 205 minutes) alcohol consumption. Ear temperatures measured at fixed intervals (-90, zero, 25, 35, 45, 55, 65, 75, 85, 115, 145, 175, 205 minutes) throughout the study in all but one subject.

Dependent Variables

- BrAC were determined by breathing into a fuel cell sensor analyzer (Alco-Sensor IV; Intoximeters, Inc., St Louis, MO). From the raw BrAC data, the time to peak, peak values, area under the blood alcohol time curve concentration (AUC; g$h/L), and elimination rate (R) for each subject and condition were calculated. AUCs were estimated using a software program (OriginLab® Corp., Northampton, MA) based on the trapezoidal rule. The alcohol elimination rate (R), expressed as the amount of alcohol eliminated per kilogram of the body per hour, was calculated as $R=\beta_{60}$/body weight.
- Ear temperatures: Measured by Thermoscan pro-LT, Braun (ThermoScan Inc., San Diego, CA).

Independent Variables

Breast pumping

Control Variables

Alcohol consumption:

- Pumped before and after drinking
- Fed and fasted
- During lactation and after lactation.

Description of Actual Data Sample:

- *Initial N:* Lactating women (N=12) who were exclusively breastfeeding three- to five-month-old infants were recruited
- *Attrition (final N):* Lactating women (N=12) who were exclusively breastfeeding three- to five-month-old infants were recruited
- *Age:* 33.0±1.2 years of age
- *Ethnicity:*
  - Six Caucasian
  - Four African American
  - Two other/mixed race/ethnic group
- *Other relevant demographics:* A mean body mass index (BMI) of 23.1±0.9kg/m^2 at the start of testing (during lactation) and 23.6±1.0kg/m^2 at the testing visit after lactation
- *Anthropometrics:* Groups were matched for age, time since parturition and drinking habits
- *Location:* Pennsylvania, US.

Summary of Results:

Table 1. Effects of Timing of Breast Pumping Stimulation Relative to Alcohol Consumption (Pumping Group), Condition (Fed and Fasted), and Reproductive State (During Lactation and After Lactation) on Alcohol Pharmacokinetics and Ear Temperatures.

	Fed				Fasted				Statistical Effects	
	PB		PA		PB		PA			
	During	After	During	After	During	After	During	After		
Outcomes	**Lactation**	**Lactation**	**Lactation**	**Lactation**	**Lactation**	**Lactation**	**Lactation**	**Lactation**	**Interaction**	**Main**
Pharmacokinetics[a]										
AUC (g.h/L)	0.64±0.06	0.59±0.06	0.82±0.07	0.84±0.07	1.25±0.08	1.27±0.05	1.39±0.10	1.37±0.06		Group: P=0.07; Condition: P<0.0001 Condition: P=0.004
Time to peak	0.97±0.12	1.01±0.13	0.82±0.14	0.92±0.15	0.58±0.07	0.44±0.05	0.62±0.08	0.68±0.06		
BrAC (h)										
Temperature[b]										
Peak temperature (°C)	36.0±0.1	36.4±0.1	36.2±0.1	37.1±0.1	35.4±0.1	36.3±0.1	36.0±0.1	36.7±0.2	State X condition: P=0.03; State X condition X group: P=0.004	Group: P=0.002; State: P=0.004; Condition: P=0.001

Nadir temperature (°C)	34.9±0.1	35.6±0.2	35.6±0.1	36.3±0.2	34.4±0.1	35.5±0.2	35.3±0.1	36.1±0.2		Group: P=0.005; State: P=0.003; Condition: P=0.008

PA=pumped after; PB=pumped before
[a]Plus-minus values represent means±SEM of seven women in group PA and five women in group PB
[b]Plus-minus values represent means±SEM of six women in group PA and five women in group PB

Figures showed:

1. BrAC time curves of the PB group were lower than the PA group curves at time 0e55 minutes when women were tested during lactation and at time 45e105 minutes when women were tested after lactation
2. Differences in BrAC between PA and PB groups were only different at one time-point
3. The differences between lactating and postlactating women's temperature response to fasting and alcohol, as depicted by delta temperature changes relative to respective baseline values.

Author Conclusion:

Lactating women metabolized alcohol differently, in part, due to the frequent breast stimulation during breastfeeding and the pronounced physiological changes with very energetically costly activity.

Reviewer Comments:

The study limitations:

- *Additional control groups (e.g., parous women who are formula feeding similarly aged infants, women tested in both pumping conditions and during both reproductive stages) were needed to separate the effect of recent parturition on ethanol metabolism*
- *Because ethanol was orally administered in the present study, the study could not differentiate the effects of reproductive stage and breast stimulation on ethanol absorption separately from their effects on elimination. Therefore, future research, using ethanol clamp or paracetamol techniques, was needed to investigate the mechanisms by which lactational state and breast stimulation affect how the drug is absorbed separately from how it is eliminated.*
- *There were better and more sensitive methods to measure the effects of alcohol ingestion on thermoregulatory responses.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes

3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes

	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes